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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,356	05/03/2001	Donald Morris	032775-041	6890

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,356	MORRIS ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,19 and 25-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☐ Claim(s) *18, 19 and 25-59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/18/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments and Amendment

1. Claims 18, 19 and 25-59 are pending.

Claims 50-59 have been added.

Claims 18, 19 and 25-59 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 50-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Applicants have added independent claim 50 and dependent claims 51-59. Claim 50 recites the limitation "...to result in oncolysis of ras-mediated neoplastic cells under conditions that does not alter the ability of the

hematopoietic cells to differentiate into each and every hematopoietic lineage." Applicants have noted that support can be found in original claims 17 and 2, as well as page 50, lines 6-15 of the specification. The Examiner has reviewed the original claims and notes that the originally filed specification only contains 22 pages (not including the claims and abstract). There is no page 50 in the specification and accordingly support for new claim 50 is not found. The Examiner has even reviewed page 5, lines 6-15 in case Applicants' erred in the listing of the page number, however no support has been found on that page. Applicants are requested to properly pointedly express in the specification by page and line number where support can be located or delete the phrase.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 50-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 50 is vague and indefinite in the recitation "under conditions that does not alter the ability of the hematopoietic cells to differentiate into each and every hematopoietic lineage". It is not clear what conditions are necessitated to not alter the ability of the hematopoietic cells to differentiate. It is not clear what properties are enveloped by the recitation "under conditions". The metes and bounds cannot be determined.

Maintained Rejections and New Grounds of Rejection

Claim Rejections - 35 USC § 103

7. The rejection of claims 18, 19, 25, 27-32, 34-40, 43-46, 49 and newly added claims 50-59 under 35 U.S.C. 103(a) as being unpatentable over Gulati (Journal of Hematotherapy 2:467-471, 1993), in view of Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS reference) and Freshney (Culture of Animal Cells: A Manual of Basic Technique, second edition, New York, NY, 1987) is maintained and made.

Applicants assert that "[t]here is no suggestion or motivation...in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the reference or to modify the combined reference teachings to arrive at the claimed invention", see Remarks submitted July 6, 2004, page 9, last paragraph. Applicants also set forth the requirements of rejections issued under 35 USC § 103 and reiterate the teachings of the cited references, see Remarks, bridging paragraph of pages 7 and 8; page 9. Applicants aver that the Examiner provides a motivation to purge, rather than a motivation to combine Gulati and Coffey et al. These points of view and arguments have been carefully considered, but found unpersuasive.

The Examiner provided several statements supporting the instant case of *prima facie* obviousness including motivation to combine Gulati and Coffey, see the Paper, first action on the merits (FAOM) mailed April 5, 2004, pages 4-6, with particularity bridging paragraph of pages 4 and 5, as well as first full paragraph of page 5. The Examiner does not solely rely on Gulati because

clinical benefits have been obtained. Gulati also reveals "[t]he success of autologous stem cell transplantation using bone marrow or peripheral blood stem cells..." and suggests "[v]arious methods... for removing (purging)...contaminants", see abstract. Gulati explains that the "[*e*]*x vivo* purging can be achieved by negative selection in which the tumor cells are eliminated, or by positive selection", see page 468, column 1, Purging techniques section. These are all suggestions and motivation to combine the teachings of Gulati, Coffey and Freshney, see rejection in its entirety in the FAOM. One of ordinary Absent evidence to the contrary it is expected that the oncolysis of ras-mediated neoplastic cells takes place under conditions that do not alter the ability of the hematopoietic cells to differentiate into each and every hematopoietic lineage.

8. The rejection of claims 18, 19, 25-29, 31-36, 38-49 and newly added claims 50-59 under 35 U.S.C. 103(a) as being unpatentable over Gulati (Journal of Hematotherapy 2:467-471, 1993), in view of Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS reference) and U.S. Patent number 6,136,307 (filed February 24, 1999/ IDS reference) is maintained and made.

Applicants' arguments for this instant rejection reflect what was presented previously in paragraph 7. Moreover, Applicants aver that patent '307 provides no motivation or suggestion to combine Gulati and Coffey. These points of view and arguments have been carefully considered, but found unpersuasive.

The Examiner provided several statements supporting the instant case of *prima facie* obviousness including motivation to combine Gulati and Coffey, see the FAOM, pages 7-9. The rejection is maintained for the reasons of record herein and established in the FAOM. Furthermore, absent evidence to the contrary it is expected that the oncolysis of ras-mediated neoplastic cells take place under conditions that do not alter the ability of the hematopoietic cells to differentiate into each and every hematopoietic lineage.

9. The rejection of claims 18, 25-29, 38-43 and newly added claims 50-54 and 56-59 under 35 U.S.C. 103(a) as being unpatentable over Nordon et al. (Artificial Organs 20(5): 396-402, May 1996), in view of Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS reference) and U.S. Patent number 6,136,307 (filed February 24, 1999/ IDS reference) is maintained and made.

Applicants reiterate statements provided by the Examiner in the FAOM and suggest what those statements meant. In conclusion, Applicants note that the MPEP and case law expressly provide that the level of skill in the art cannot be relied upon to provide the suggestion to combine references and there is no motivation or suggestion to combine the prior art references. These points of view have been carefully reviewed and considered, but found unpersuasive.

Nordon establishes well known, as well as art known methodologies of ex vivo expansion technology for the development of new cellular products for the treatment of cancer, see title and abstract. Nordon also makes reference to future technologies, developing novel cell-based therapies for the treatment of

malignancy and sets forth proof that ex vivo manipulation of cell subsets is routine in the art, see page 400 conclusions section. The inference and teachings set forth by Nordon in combination with the secondary references establishes *prima facie* case obviousness. The rejection is maintained for the reasons of record herein and established in the FAOM. Furthermore, absent evidence to the contrary it is expected that the oncolysis of ras-mediated neoplastic cells takes place under conditions that do not alter the ability of the hematopoietic cells to differentiate into each and every hematopoietic lineage.

10. The rejection of claims 18, 19, 25-49 and newly added claims 50-59 under 35 U.S.C. 103(a) as being unpatentable over Nordon et al. (Artificial Organs 20(5): 396-402, May 1996), in view of Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS reference), U.S. Patent number 5,861,159 (January 19, 1999) and U.S. Patent number 6,136,307 (filed February 24, 1999/ IDS reference) is maintained and made.

Applicants' arguments are the same as noted in paragraph 9, aside from the arguments that "the '159 patent does not cure the deficiency of lack of motivation or suggestion to combine Nordon et al. and Coffey et al". Applicants reiterate statements provided by the Examiner in the FAOM and suggest what those statements meant. In conclusion, Applicants note that the MPEP and case law expressly provide that the level of skill in the art cannot be relied upon to provide the suggestion to combine references and there is no motivation or

suggestion to combine the prior art references. These points of view have been carefully reviewed and considered, but found unpersuasive.

Nordon establishes well known, as well as art known methodologies of ex vivo expansion technology for the development of new cellular products for the treatment of cancer, see title and abstract. Nordon also makes reference to future technologies, developing novel cell-based therapies for the treatment of malignancy and sets forth proof that ex vivo manipulation of cell subsets is routine in the art, see page 400 conclusions section. The inference and teachings set forth by Nordon in combination with the secondary references establishes *prima facie* case obviousness. It clear in patent '159 immune system stimulating agents taught in the said patent would be effective in preventing tumor growth, tumor metastasis and tumor regression in a subject. The previous action clearly established that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to implement the teachings of all the references in the method of preparing a cellular composition including immune system stimulating agents for autologous transplantation in order to destroy the neoplastic cells and the motivation to do so, as well as one of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings well known in the art the manufacture of anti-tumor medicaments incorporating anti-cancer agents is efficacious for the in vivo treatment of cancer and the potentiation of a subjects' immune response. Accordingly, the rejection is maintained for the reasons of record herein and established in the FAOM.

Furthermore, absent evidence to the contrary it is expected that the oncolysis of ras-mediated neoplastic cells takes place under conditions that do not alter the ability of the hematopoietic cells to differentiate into each and every hematopoietic lineage.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner works a flexible schedule, however

she can normally be reached between the hours of 6:30 am to 5:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
13 September 2004